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09/302,239	04/29/1999	GARY L. NELSESTUEN	09531/005001	6644

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EXAMINER	
SCHNIZER, HOLLY G	
ART UNIT	PAPER NUMBER
1653	26

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Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No. 09/302,239	Applicant(s) NELSESTUEN, GARY L.	
	Examiner Holly Schnizer	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-14,16,17 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7-14,16,17 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

The Amendment filed February 19, 2003 has been entered and considered. Claim 6 has been cancelled and Claims 23-27 have been added. Therefore, Claims 1, 3-5, 7-14, 16, 17, and 23-27 are pending and have been considered in this Office Action.

Drawings

The drawings filed July 23, 2002 have been approved by the draftsperson.

Rejections/Objections Withdrawn

The rejection of Claims 1, 3-14, 16, and 17 under 35 U.S.C. 112 second paragraph as being indefinite for the recitation of substitutions at particular amino acid positions without placing the positions within the context of a sequence is withdrawn in light of the amendment.

The objection of Claim 11 under 37 CFR 1.75 as being a substantial duplicate of claim 6 is withdrawn in light of the cancellation of Claim 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, 7-14, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is still confusing as to how many substitutions may be made. The claim states "at least one amino acid substitution" implying that more than one substitution in a single protein may be made. However, the claim states that the "at least one amino acid substitution" is at position 11 or 29 implying that either one or the other position may have a substitution. Such inconsistency causes confusion in the dependent claims 3-5, 7-14, and 16 as well. Clarification is required. If more than one substitution in a single polypeptide is intended (at both positions 10 and 28 for example) then changing "or" to "and/or" is suggested.

Double Patenting

Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 7-14, 16-17, and new claims 23-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 6,017,882.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

The examiner acknowledges Applicants indication that a terminal disclaimer will be submitted upon notification of allowable subject matter. However, the rejection still stands until such a submission.

Claim 1 of U.S. Patent No. 6,017,882 recites a vitamin K-dependent polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native vitamin K-dependent polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue 11, 12, 29, or 34, and wherein said polypeptide increases clot formation. Claim 4 depends from Claim 1 with the addition that the polypeptide comprises an additional substitution at

position 33. Claims 1 and 4 differ from the present claims herein in that they are drawn to the genus of vitamin K-dependent proteins and not the specific members such as Factor VII claimed herein. Claims 1 and 4 also differ in that they include the additional limitation that the polypeptide must increase clot formation. Claims 1 and 4 differ from the dependent claims herein in that it fails to recite the specific amino acids to be substituted at the specific positions claimed. However, U.S. Patent No. 6,017,822 teaches that factor VII is a vitamin K dependent polypeptide that may be modified to enhance membrane binding affinity (Col. 7-8 and Ex. 1 and 2) and that modifying factor VII would provide the benefit of lowering the dosage necessary in treatment (Col. 2, lines 35-40). U.S. Patent No. 6,017,822 also teaches that substituting glutamine, glutamate or aspartate at position 10; phenylalanine at position 29; and/or aspartate at position 33 (all positions relative to the factor VII sequence) would result in the desired effect (enhancement of membrane binding; see Col. 7, lines 30-50). Moreover, specifically substituting glutamine at position 11 and glutamate at position 33 is disclosed as resulting in a polypeptide with much higher affinity for membranes and having much higher activity in autoactivation, in factor Xa generation and in several blood clotting assays (Col. 7, lines 55-57). Therefore, it would have been obvious to select factor VII from the vitamin K dependent proteins claimed in U.S. Patent No. 6.017,882 and make the specific amino acid changes claimed in the present application. One having ordinary skill in the art would have been motivated to choose factor VII and the specific modifications presently claimed since U.S. Patent No. 6, 017, 882 teaches that these modifications result in enhanced membrane binding and that enhanced

membrane binding in factor VII would be desirable since it would allow for administration of lower doses of factor VII in therapy.

The examiner acknowledges that a restriction requirement was made in the parent application, however, the restriction appears to have been made subject to non-allowance of a generic claim (see Paper No. 3 in Appl. No. 08/955,636, see specifically p. 4, lines 12-14 of the Office Action) and the generic claim (to vitamin K-dependent polypeptides) was allowed. Thus, the double patenting rejection above applies.

New Rejection Prompted by the Submission of the IDS filed February 19, 2003

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 7, 8, 9, 13, and 23-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheung et al. (Thromb. Res. (1995) 79(2):199-206; Ref. AQ in IDS of Paper No. 24).

Cheung et al. disclose a factor VII polypeptide comprising a modified GLA domain comprising a substitution of glutamine at position 10 of SEQ ID NO:3 or 4 and a glutamate at position 32 of SEQ ID NO:3 or 4 (see mutant 4 in Fig. 1, page 202). Chueng et al. do not teach that the mutant factor VII disclosed therein has enhanced membrane binding affinity or activity relative to the corresponding native factor VII

(sequence shown in first line of figure). However, the issue at hand is not whether Chueng et al. knew that the mutant protein had properties presently claimed but whether Chueng et al. disclose a product that is patentably indistinguishable from that presently claimed. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. (see MPEP 2111.03 and In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977 cited therein). In the present case, the factor VII mutant 4 of Chuang et al. meets all of the structural limitations of Claims 1, 3, 4, 7, 8, 13, and 23-27. The functional properties of a protein are dependent on its sequence. Therefore, it would be inherent that the mutant 4 of Chuang et al. would have the claimed functional characteristics (enhanced membrane binding and activity). Chuang et al. teach that the mutant proteins bind to a factor VII monoclonal antibody and suggest that the folding of factor VII is not disturbed by the mutations (p. 202, 1st paragraph). Factor VII mutant 4 has mutations that enhance membrane binding and activity (the substitution of Gln at position 10 and the substitution of Glu at position 32 shown in Ex. 1 of the present Specification to have enhanced binding and activity). Factor VII mutant 4 of Chuang et al. has additional mutations at positions 8, 9, 33, 34, 38, all of which are changes from a human factor VII amino acid to a human factor IX amino acid at the corresponding position. The factor IX Gla domain has enhance membrane binding as compared to that of factor VII, therefore, it would be inherent that a protein with a Gla domain more closely resembling that of factor IX would have enhanced membrane binding. Furthermore, there is a correlation between membrane affinity and the net negative

charge of the surface amino acids (see p. 47 and Fig. 11 of the Specification) and all of the mutations of mutant 4 of Chuang et al. either do not change the charge at all (positions 8 and 34), change the amino acid from a human factor VII amino acid to that found in bovine factor VII (position 33) or change the amino acid to provide an overall more negative charge (change from positive to negative or neutral and from neutral to negative)(positions 9, 38, and 39. Therefore, the Gla domain of mutant 4 of Chuang et al. has a more negative net charge than the native human factor VII, which is correlated with enhanced membrane affinity, and it has a sequence more closely resembling human factor IX, which has enhanced membrane binding affinity than factor VII. Thus, the factor VII mutant 4 of Chuang et al. has all of the structural limitations of the claim and inherently has all of the functional limitations of the claims.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. In addition, Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on February 19, 2003 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Monday through Wednesday from 8 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

HS

Holly Schnizer
May 7, 2003

Christopher S. F. Low

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